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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/028,224	BENSON ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-78* is/are pending in the application.

4a) Of the above claim(s) *1-53,77 and 78* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1-78 are pending in the application.

[2] Applicant's amendment to the claims, filed February 12, 2004, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] Applicants' amendment to the specification, filed February 12, 2004, is acknowledged.

[4] Receipt of an Information Disclosure Statement, filed February 12, 2004, is acknowledged.

[5] Claims 1-53 and 77-78 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

[6] Claims 54-76 are being examined on the merits.

[7] Applicants' arguments filed on February 12, 2004 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[8] The text of those sections of Title 35, U.S. Code not included in the instant action can be found in a prior Office action.

Information Disclosure Statement

[9] All references cited on the information disclosure statement (IDS) filed February 12, 2004 have been considered by the examiner. A copy of the IDS is attached to the instant Office action.

Specification/Informalities

[10] In view of applicants' amendment to the specification, the notice to comply with the sequence requirements and the objections to the specification as set forth in items [11]-[14] of the Office action mailed August 12, 2003 are withdrawn.

Claim Objections

[11] In view of applicants' amendment to claims 55 and 58, the objection to the claims as set forth in item [15] of the Office action mailed August 12, 2003 is withdrawn.

Claim Rejections - 35 USC § 112, First Paragraph

[12] The written description rejection of claims 54-76 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth in item [21] of the Office action mailed August 12, 2003 and for the reasons stated below. The examiner maintains the position that the single representative species of the genus of human beta secretases crystallized in the presence of a genus of inhibitors by the method of claims 54-71, i.e., the human beta secretase of SEQ ID NO:1 crystallized in the presence of the inhibitor of Figure 1, and the genus of beta secretase crystals of claims 72-76 as

disclosed in the specification, i.e., a crystal of the purified human beta secretase of SEQ ID NO:1 having a trigonal space group symmetry of $P3_221$ and the unit cell dimensions of a=b=112±20, c=110±20, and $\alpha=\beta=90^{\circ}$ and $\gamma=120^{\circ}$ or a=b=99±35, c=117±35, and $\alpha=\beta=90^{\circ}$ and $\gamma=120^{\circ}$ produced using purified human beta secretase of SEQ ID NO:1 in the presence of the inhibitor of Figure 1, fails to represent the entire genus.

Applicants argue the specification provides an adequate written description and support for the claimed invention. Applicants argue that in view of Annex 3 of the "Trilateral Project WM4, Comparative studies in new technologies, Theme: Comparative study on 'protein 3-dimensional (3-D) structure related claims'" and the disclosure of the structure of beta secretase and the atomic coordinates thereof, the specification is sufficient to describe the genus of claimed/recited beta secretase crystals. Applicants' argument is not found persuasive.

The issue at hand is whether the single disclosed species as stated above is sufficient to represent the entire genus of claimed or recited beta secretases of claims 54-74, inhibitors thereof as recited in claims 54-71, and crystals thereof as recited in claims 72-76. MPEP § 2163 states that when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus and that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus". In this case, the genus of claimed or recited beta secretase crystals of claims 54-76 and inhibitors thereof as recited in claims 54-71 encompasses species that are WIDELY variant. With respect to the beta secretase

polypeptides, the art acknowledges that there are multiple distinct structures of "human beta secretase" (see for example, Farzan et al. *Proc Natl Acad Sci, USA* 97:9712-9717 and Ehehalt et al. *Biochem Biophys Res Commun* 293:30-37; cited in a previous Office action) and also, based on the specification, it appears that the terms "beta secretase" and "human beta secretase" are meant to encompass not only those beta secretases that are naturally occurring, but to also encompass mutants and variants thereof (see page 15, lines 17-20; pages 25-26; and pages 28-29). Regarding the inhibitors of beta secretase as recited in claims 54-71, the specification discloses only a single beta secretase inhibitor that, when in the presence of human beta secretase and under the proper conditions, will result in the formation of a crystal of human beta secretase. With respect to the crystals of beta secretase, the specification acknowledges that "human beta secretase can crystallize in more than one form" (see page 29, line 21 of the instant specficiation) and a trigonal space group requires a=b in the unit cell dimensions, however, the unit cell dimensions of a and b as recited in claims 73 and 74 are not required to be equivalent. Regarding applicants' citation of Case 4 of Annex 3 of the "Trilateral Project WM4, Comparative studies in new technologies, Theme: Comparative study on 'protein 3-dimensional (3-D) structure related claims'" (see excerpt at Appendix A), it is noted that none of the claims are limited to the recitation of a crystal having specific unit cell dimensions. In contrast to Case 4, claims 72-76 recite a crystal of beta secretase having a broad range of unit cell dimensions, i.e., a=about 77Å to about 147Å, b=77Å to about 147Å, and c=77Å to about 147Å. It should also be noted that claims 72-74 do not limit the source of the beta secretase and are instead

drawn to a crystal of a beta secretase from any source. As such, the disclosure of the single representative species as described above is insufficient to be representative of the attributes and features of all species encompassed by the genus of claimed or recited beta secretases and inhibitors and crystals thereof. Given the lack of description of a representative number of species, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[13] The scope of enablement rejection of claims 54-76 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth in item [22] of the Office action mailed August 12, 2003 and for the reasons stated below. The examiner maintains his position that the specification, while being enabling for a method for crystallizing the human beta secretase of SEQ ID NO:1 complexed with the human beta secretase inhibitor of Figure 1 by preparing purified human beta secretase of SEQ ID NO:1 in the presence of the inhibitor of Figure 1 to a final concentration of 18-40 mg/mL beta secretase protein and 2 mM inhibitor and crystallizing human beta secretase using the hanging drop method in a solution of 17-20% PEG 3000, 0.1 M sodium acetate, pH 4.5 at 20 degrees Celsius and optionally wherein the solution contains 10% glycerol or 10% ethylene glycol and a crystal of the human beta secretase of SEQ ID NO:1 having a trigonal space group symmetry of $P3_221$ and the unit cell dimensions of a=b=112±20, c=110±20, and $\alpha=\beta=90^\circ$ and $\gamma=120^\circ$ or a=b=99±35, c=117±35, and $\alpha=\beta=90^\circ$ and $\gamma=120^\circ$, does not reasonably provide enablement for a method for crystallizing any human beta secretase molecule or molecular complex by preparing purified human beta

secretase in the presence of any inhibitor and crystallizing human beta secretase from any solution having a pH of about 3.5-5.5 and optionally under the conditions as recited in claims 55-71 or all crystals of beta secretase from any source having the trigonal space group symmetry $P3_221$ and/or the unit cell dimensions as recited in claim 73, and optionally wherein the beta secretase is SEQ ID NO:1 with at least one methionine replaced with selenomethionine.

Applicants argue the specification describes a method for crystallizing human beta secretase and includes working examples of such, provides methods of using the claimed crystals, and the examiner has not provided any reason to doubt the alleged objective truth of the disclosure.

There is no dispute that the specification describes a method for crystallizing human beta secretase, includes working examples of such, and provides methods of using the claimed crystals. However, the issue at hand is whether the specification enables the entire scope of claimed crystals and methods – not just those working examples disclosed in the specification. It is the examiner's position that the specification does not enable the full scope of claimed methods and crystals for the reasons stated herein.

Applicants argue that the examiner's support (Chopra et al., Tang et al., and Hong et al.; cited in a previous Office action) for showing the unpredictability associated with altering the crystallization parameters of a given protein with an expectation of obtaining a protein crystal with a *specific* space group symmetry or unit cell dimensions is inapposite to the instant rejection as these references describe crystallization of beta

secretase at a pH outside the claimed range of pH values, i.e., 3.5 to 5.5. Applicants' argument is not found persuasive.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the formation of crystals at a pH range of 3.5 to 5.5) are not recited in claim(s) 72-76. Furthermore, contrary to applicants' assertions, the references of Chopra et al., Tang et al., and Hong et al. fully support the examiner's showing of unpredictability. These references were applied to support the teachings of Branden et al. (cited in a previous Office action), who teach that protein crystallization is usually quite difficult to achieve and the formation of protein crystals is critically dependent on a number of different parameters, including pH, temperature, protein concentration, the nature of the solvent and precipitant, as well as the presence of added ions and ligands to the protein (page 375, middle) and that even small changes in the crystallization parameters, e.g., pH, can cause the molecules to pack in different ways to produce different crystal forms (page 375, bottom). It should be noted that applicants do not dispute the teachings of Branden et al., Chopra et al., Tang et al., and Hong et al. Further evidence of such unpredictability is provided by Drenth ("Principles of Protein X-ray Crystallography," 2nd Ed., Springer-Verlag NY Inc., 1994; cited by applicants in the IDS filed February 12, 2004) who teaches that "[o]btaining suitable single crystals is the least understood step in the X-ray structural analysis of a protein. The science of protein crystallization is an underdeveloped area... ...Protein crystallization is mainly a trial-and-error procedure" (page 1). Additional evidence of such unpredictability is provided by Beyer et al. (US

Patent Application Publication 2004/0014194 A1), who teach crystallization of human beta secretase in a buffer having pH 4.0 in the presence (Example 6) and absence (Example 9) of an inhibitor resulted in crystals having a space group ($P2_12_12_1$) and unit cell dimensions that are distinct from the crystals as disclosed in the instant specification.

Claims 54-76 are not limited by the composition of the crystallization buffer and the specification fails to provide guidance for altering any parameters of the disclosed crystallization buffer with an expectation of obtaining the desired crystals. Thus in view of these teachings, a skilled artisan would recognize that even slight changes in a single parameter for protein crystallization can result in crystals – if any at all – that are distinct in structure having different space group symmetry and unit cell dimensions. The level of unpredictability is further compounded by the numerous parameters that can be altered, e.g., protein concentration, pH, temperature, buffer composition.

Regarding claim 76, applicants argue one of skill in the art would not necessarily expect replacement of methionine with selenomethionine to result in different packing properties as selenomethionine replacement is well known in the art and cite Hendrickson et al. (cited in the IDS filed February 12, 2004) in support of their argument. Applicants' argument is not found persuasive.

It should be noted that Hendrickson et al. teach production of recombinant selenomethionyl *E. coli* thioredoxin and crystallization thereof. Hendrickson et al. do not address the crystallization of selenomethionyl beta secretase and whether selenomethionine replacement of methionine residues results in altered crystal packing.

At the time of the invention, neither the specification nor the prior art provided any guidance as to whether selenomethionine replacment in a beta secretase would alter the crystal packing and in view of the teachings of Branden et al. and Drenth, one of skill in the art would have recognized the unpredictability that replacing methionine with selenomethionine would result in a crystal having the desired space group symmetry.

Applicants argue that in view of the specification, one of skill in the art would be able to make and use the entire scope of the claimed invention. Applicants argue that the teachings of the specification would enable a skilled artisan to make other crystals of human beta secretase without undue experimentation by, for example, using cross-seeding techniques. Applicants' argument is not found persuasive.

Based on the analysis of the factors of *In re Wands* as set forth in a previous Office action (see pages 10-14 of the Office action mailed August 12, 2003) and reiterated (in part) above, undue experimentation is clearly required to make and use the full scope of the claimed invention. While methods of protein crystallization are known, it is *not* routine in the art to screen the vast array of conditions for crystallizing a human beta secretase protein or to crystallize any beta secretase as encompassed by the instant claims. Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Double Patenting Rejection(s)

[14] A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

[15] The provisional double patenting rejection of claims 54-76 under 35 U.S.C. 101 as claiming the same invention as that of claims 1-23 of copending Application No. 10/027,277 (hereafter referred to as "Application '277") is maintained for the reasons of record as set forth in item [24] of the Office action mailed August 12, 2003. The examiner maintains the position that claims 54-76 are identical in scope to claims 1-23 of Application '277. Applicants do not dispute the examiner's position as stated above. Applicants assert that "in the event this rejection is maintained, Applicants will provide an appropriate response" (see page 26, top of the amendment filed February 12, 2004. Thus, an appropriate response is requested.

[16] The provisional double patenting rejection of claims 54, 56, and 72-76 under 35 U.S.C. 101 as claiming the same invention as that of claims 4, 5, and 24-28 of copending Application No. 10/144,441 (hereafter referred to as "Application '441") is maintained for the reasons of record as set forth in item [25] of the Office action mailed August 12, 2003. The examiner maintains the position that claims 54, 56, and 72-76 are identical in scope to claims 4, 5, and 24-28 of Application '441. Applicants do not

dispute the examiner's position as stated above. Applicants assert that "in the event this rejection is maintained, Applicants will provide an appropriate response" (see page 26, top of the amendment filed February 12, 2004. Thus, an appropriate response is requested.

[17] The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

[18] The provisional double patenting rejection of claims 54, 55, and 57-71 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 6-23 of copending Application No. 10/144,441 (hereafter referred to as "Application '441") for the reasons of record set forth in item [27] of the Office action mailed August 12, 2003. The examiner maintains the position that the specification of Application '441 supports an embodiment that would anticipate claim 54 herein, i.e., a pH range of about 3.5 to about 5.5 (see for example claim 4 of Application '441) and that claims 54, 55, and 57-71 cannot be considered to be patentably distinct over claims 1-3 and 6-23 of Application '441 when there is a specifically recited embodiment in Application '441 that would anticipate claims 54, 55, and 57-71 of the instant

application. Applicants do not dispute the examiner's position as stated above. Applicants assert that "in the event this rejection is maintained, Applicants will provide an appropriate response" (see page 26, middle, of the amendment filed February 12, 2004. Thus, an appropriate response is requested.

[19] Claims 54-69 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7-23 of copending Application No. 10/143,502 (hereafter referred to as "Application '502"). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 54-69 of the instant application and claims 7-23 of Application '502 are both directed to methods for crystallizing a human beta secretase. The claims differ in that the claims of the instant application are limited to crystallizing in the presence of an inhibitor, while the claims of Application '502 are limited to crystallizing in the presence of a potential modifier. The claims further differ in that in the pH of the crystallization solution of claim 54 of the instant application is about 3.5 to about 5.5 whereas the pH of the solution of claim 7 of Application '502 is about 3.5 to about 5.6. The specification of Application '502 supports an embodiment of a potential modifier as being an inhibitor

of human beta secretase. For example, the specification of Application '502 states, "Figure 1 is an illustration of the chemical structure of a modifier used in co-crystallization experiments" (page 7) and Figure 1 of Application '502 discloses the structure of a compound that is identical to Figure 1 of the instant application, which is described as follows: "Figure 1 is an illustration of the chemical structure of an inhibitor used in co-crystallization experiments" (page 11). The specification of Application '502 supports an embodiment that would anticipate a pH range of about 3.5 to about 5.5. For example, claim 8 of Application '502 recites a pH range of about 4.0 to about 4.7. Claims 54-69 cannot be considered to be patentably distinct over claims 7-23 of Application '502 when there is a specifically disclosed embodiment in Application '502 that falls within the scope of claims 54-69 because it would have been obvious to one of ordinary skill in the art to modify the methods of claims 7-23 of Application '502 by selecting a specifically disclosed embodiment that supports these claims, i.e., the crystallization of human beta secretase in the presence of the inhibitor of Figure 1 in a solution of about pH 4.0 to about 4.7 as disclosed in Application '502. One of ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being a preferred embodiment within the claims.

[20] Claims 54-67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-26 of copending Application No. 10/143,723 (hereafter referred to as "Application '723"). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the

reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 54-67 of the instant application and claims 12-26 of Application '723 are both directed to methods for crystallizing a human beta secretase. The claims differ in that the claims of the instant application are limited to crystallizing in the presence of an inhibitor, while the claims of Application '723 are limited to crystallizing in the presence of a potential modifier. The claims further differ in that in the pH of the crystallization solution of claim 54 of the instant application is about 3.5 to about 5.5, whereas the pH of the solution of claim 12 of Application '723 is about 4.5 to about 5.6, the pH of the solution of claim 13 is unlimited, or the pH of claim 16 of Application '723 is about 4.0 to about 6.5. The specification of Application '723 supports an embodiment of the recited potential modifier as being an inhibitor of human beta secretase. For example, the specification of Application '723 discloses that "Figure 1 is an illustration of the chemical structure of an inhibitor used in co-crystallization experiments" (page 8) and Figure 1 of Application '723 discloses the structure of a compound that is identical to Figure 1 of the instant application, which is described as an inhibitor of human beta secretase. Also, the specification of Application '723 supports an embodiment that would anticipate a pH in the range of about 3.5 to about 5.5. For example, the specification of Application '723 discloses that crystals of human beta secretase in the presence of inhibitor were

obtained in a solution of pH 4.5 containing 0.1 mM ammonium sulfate (page 51). Claims 54-67 cannot be considered to be patentably distinct over claims 12-26 of Application '723 when there is a specifically disclosed embodiment in Application '723 that falls within the scope of claim 54-67 because it would have been obvious to one of ordinary skill in the art to modify the methods of claims 12-26 of Application '723 by selecting a specifically disclosed embodiment that supports these claims, i.e., the crystallization of human beta secretase in the presence of the inhibitor of Figure 1 in a solution of pH 4.5 containing 0.1 mM ammonium sulfate as disclosed in Application '723. One of ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being a preferred embodiment within the claims.

Conclusion

[21] Status of the claims:

- Claims 1-78 are pending
- Claims 1-53, 77, and 78 are withdrawn from consideration.
- Claims 54-76 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (703) 746-5078. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman
Patent Examiner
Art Unit 1652

03-15-04

APPENDIX A

Case 4: Crystals of known proteins

[Claim]

A crystalline form of protein P having unit cell dimensions of a=4.0nm, b= 7.8nm, and c= 11.0nm.

[Background]

-A nucleotide sequence encoding the amino acid sequence of protein P was known in the art.

-The description explains that administering protein P was previously known to result in lowering blood pressure.

-The inventors assert they have newly produced a stable crystalline form of protein P.

-Protein P in crystalline form is inactive.

-The description gives experimental data with explanations of how to make the crystals.

-Common prior art methods used in protein P crystallization were unsuccessful, and there was clearly a technical difficulty in producing the claimed crystalline form of protein P.

[Prior art]

-There was no prior art reference teaching or suggesting a crystal of protein P or related proteins.

-There was no prior art reference concerning the crystallization method of protein P.